

Easy Pathology

— Dr. Abdelrahman Khalifa —

Liver & Gall Bladder



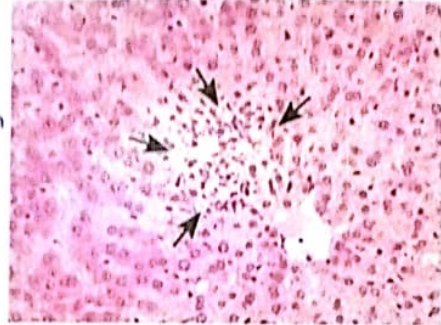
Ain Shams 2017 - 2018

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Liver cell necrosis

1. **Focal or spotty** Cytolysis (necrosis), or apoptosis, of small number of cells away from portal tracts. (*inflammatory cells*)
 - **Acute & chronic** viral hepatitis
2. **Zonal** (death of hepatocytes in specific zone)
 - **Centrizonal** (zone 3) *around Central vein*
 - **Acute & chronic** viral hepatitis
 - CVC, toxicity (CCL4, paracetamol)
 - **Midzonal** (zone 2) *- (CVC)*
 - **Yellow** fever
 - **Interface hepatitis (Piecemeal necrosis)** (patchy apoptosis & few necrosis & inflammation at the interface zone) *peripheral zone' around portal tract*
 - Active hepatitis (in **Chronic** hepatitis – **severe acute** hepatitis)
3. **Confluent** (death of large number of cells around **central vein**) → *Autoimmune diseases*
4. **Bridging necrosis** (a bridge of necrotic cells → **P-P, P-C, C-C**)
 - **Acute & Chronic** hepatitis
5. **Submassive & massive necrosis** Entire lobule or Multilobular
 - Severe **fulminant hepatitis** (viral, toxic, autoimmune) → liver failure



Effects of liver necrosis: elevated enzymes (**SGPT, SGOT**) – **Cirrhosis** & liver failure in severe cases (e.g. massive necrosis) *ALT & AST* & *regeneration + fibrosis*

Liver Viruses

HAV	HBV	HCV	HDV	HEV
RNA	DNA	RNA	RNA	RNA
ingestion	Parental – sexual – Body fluids – during labour	Parental	Parental On top of <u>HBV</u> infection	ingestion
IP : 2-6 wks	4-26 wks	2-26 wks	4-26 wks	2-6 wks
Acute only -----	Acute & chronic(10%) Cirrhosis & HCC	Acute & chronic(80%) Cirrhosis & HCC	Acute & chronic(5%-70%) Cirrhosis & HCC	Acute only -----

Acute viral hepatitis

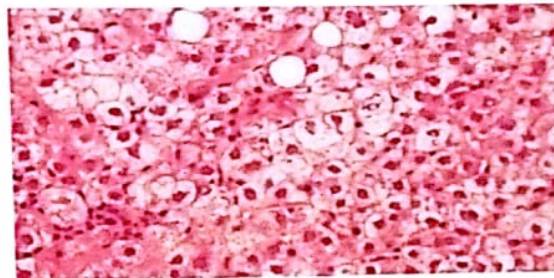
Aetiology: All hepatic viruses, **HAV** the most common (ingestion), common in **children**.

Gross: Large – **green** (due to cholestasis) → stasis of bile inside hepatocytes & obstruction of bile canaliculi

Micro:

- P.T.: ^{Fibrous Tissue} mononeuclear inflammatory cells with excess lymphocytes (?)
↳ Portal tract
- Parenchyma:
 - **Degeneration** : Hydropic ballooning – Fatty changes - Cholestasis
 - **Necrosis**: Spotty– bridging – Centrizonal – Interface hepatitis
 - **Apoptosis** (councilman bodies)
 - Sinusoidal Kupffer cell proliferation (containing necrotic debris)
 - **Regeneration** of hepatocytes
 - Lobular disarray

"degeneration"
& swelling



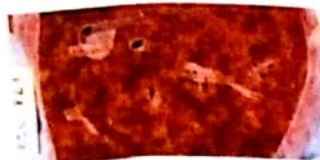
C/P:

- **Pre-icteric:** FAHM, abdominal pain, vomiting
- **Icteric:** **Jaundice**
- **Post icteric:** Recovery within 4-6 wks
In some cases of **HBV** : **Rash** & **arthralgia**
(immune reaction)



Fate & complications

- **Resolution** in all cases of HAV & HEV.
- Carrier, or Chronic in HBV (10%) & HCV (80%) → Cirrhosis (20%) or HCC
- **Acute Fulminant hepatitis:**
 - Un-explained (1%)
 - Massive **necrosis** & hemorrhage → hepatic encephalopathy & **coma** (fatal)



Chronic hepatitis

Persistent **clinical**, **laboratory** & **histological** evidence of hepatitis for more than **6 months**

Aetiology:

- HBV, HCV (α -1-antitrypsin) deficiency *Protect the lung from elastase enzyme*
- Alcoholic, Alpha1ATD, Autoimmune, Drug, Metabolic (Wilson, hemochromatosis) *Cu Fe*

Micro: its accumulation inside hepatocytes $\rightarrow$ chronic inflammation

- **Similar to Acute** (enumerate)
- Dysplasia
- **Fibrosis**: Portal $\rightarrow$ Periportal $\rightarrow$ bridging fibrosis $\rightarrow$ Cirrhosis
- **Specific findings**:

- **In (HBV):**

- **Ground glass** cytoplasm (granular HBsAg), **Orcein +ve**

- **In (HCV)**

- Steatosis
- **lymphoid follicles** in portal tracts
- Bile duct injury

- **In Alcoholic hepatitis:** *hyalinos (Protein)*

- **Mallory bodies**, **neutrophils** & centrilobular **steatosis**

- **Autoimmune** *Anti Sm, Actin* (+ve ASMA & ANA) antinuclear Abs

- Clusters of **Plasma** cells, **Confluent** necrosis

- **Drug-induced:**

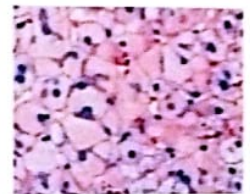
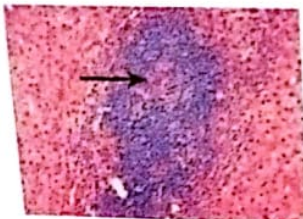
- **Eosinophils** – **Epithelioid granuloma** -centrilobular **steatosis**

- **Wilson**

- **Kayser-Fleischer** brown corneal ring
- low serum **ceruloplasmin**
- Brown granules of **copper** (stained by Orcein)

- **Alpha1 ATD** (neonatal cholestasis – Adult emphysema)

- Alpha1 AT granules (**PAS +ve**)

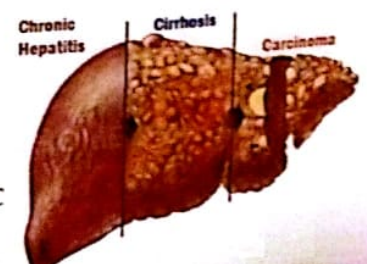


Grading & staging:

Grading: (activity) means **inflammation** & **necrosis** (1-18)

Staging: **Fibrosis** (1-6)

Fate & complications: Carrier – Cirrhosis – Liver failure – HCC

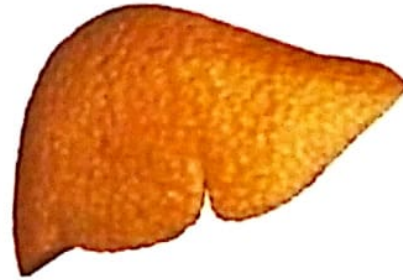


Liver Cirrhosis

Diffuse liver disease, characterized by liver necrosis followed by **regenerative nodules**, surrounded by **fibrosis**, with disturbed architecture, & disturbed normal **vasculature**

Types/Aetiology:

- * **Alcoholic**
 - **Alpha1 ATD**
- * **Biliary** (1ry – 2ry) *cholestasis*
 - *Post-hepatic viral hepatitis*
 - *Post-necrotic drugs / toxins*
- * **Cardiac** *CVC (Right sided)*
 - **Cryptogenic idiopathic**
- * **Metabolic** (Wilson, Hemochromatosis, Glycogen storage type4, Galactosemia, Tyrosenemia)



* *large liver*

Pathogenesis

Injury of hepatocytes, **endothelial** cells, or **Kupffer** cells → **TNF, IL-1 & F.R.** → activation of **Eto** cells (*fat-storing stellate cells in space of Disse*) → transform into **Myofibroblasts** → secrete **TGF-B & Collagen I & III** in liver lobules
NB. Collagen I, III, V, XI are normally found in capsule & portal tracts. Type IV only is seen in sinusoids.

Gross:

- **Size:** *retracted dt fibrosis* - **Reduced** - **enlarged** in (Alcoholic ? – Biliary ? – Cardiac ? – Metabolic ?)
- **Surface:** **Nodular**
- **Color:** grayish – except (Alcoholic → **yellow** , Biliary → green, Cardiac → **nutmeg**)
- **C/S:** (morphological classification)
 - 1-**Micronodular** (nodules **3mm- 1cm** or less) **Alcoholic, Hemochromatosis**
 - 2-**Macronodular** (> **1cm**, in **posthepatic, postnecrotic** , Autoimmune) ⇒ *PreCancerous*
 - 3-**Mixed**
- **Consistency:** **Firm**

Microscopic picture of cirrhosis:

- Liver cell **necrosis**
- Formation of **regeneration nodules** of normal hepatocytes
- Nodules are **surrounded by fibrosis**
- Fibrous septa are infiltrated with **chronic inflammatory** cells
- Disturbed **architecture**
- Disturbed normal **vasculature**
- **Specific** microscopic findings (according to the cause):
 - Alcoholic → *enumerate ?*
 - Alpha1 ATD → **Alpha1 AT granules**



- HCV → enumerate ? HBV → ground-glass hepatocytes
- Biliary → cholestasis
- Cardiac → picture of CVC
- Metabolic → deposited iron, or copper

Biliary cirrhosis

1ry	2ry
<u>Intra-hepatic bile duct damage</u>	<u>Extra-hepatic biliary obstruction</u>
Autoimmune Anti-mitochondrial Ab (AMA) More in Females 20-40 y	Congenital (biliary atresia) Inflammation & fibrosis Stones Tumors (e.g. cancer head of pancreas)
<u>Gross:</u> describe (?) <i>large-green-nodular</i>	<u>Gross:</u> the same (?)
<u>Micro:</u> Stage of Florid <u>duct lesion</u> → bile ducts damage & excess plasma cells Stage of <u>Ductular proliferation & granuloma</u> Stage of Scar & <u>fibrosis</u> of portal tracts Stage of <u>Cirrhosis</u> describe (?)	<u>Micro:</u> Accumulated <u>bile plugs</u> in bile ducts + Cirrhosis describe (?)

Alcoholic cirrhosis (Laennec's, or nutritional)

- Alcohol → Acetaldehyde → liver cell necrosis
- Grossdescribe? Microscopicdescribe?

*large
Yellow (steatosis)
Mallory bodies
neutrophils*

Complications of cirrhosis

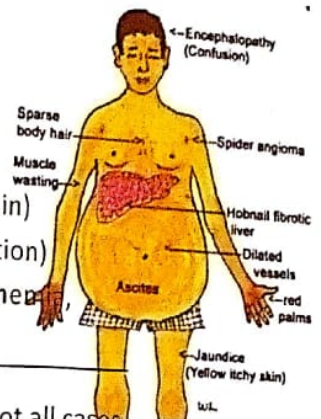
1. Portal hypertension > 10 mm Hg

- **Causes:** regenerative **nodules** + intrahepatic **A-V shunts** + production of **Nitric oxide** (hyperdynamic circulation)
- **Effects:**
 - Open **port-systemic veins** (e.g. varices → hematemesis)
 - **Ascitis** (due to **hydrostatic** portal pressure + **hypoproteinemia** + **hyperaldosteronism**)
 - **Splenomegaly** → **hypersplenism** (pancytopenia & bleeding tendency)
 - **GIT congestion** → malnutrition

2. HCC

3. Liver cell failure

1. **Ammonia** encephalopathy → Coma
2. **Bleeding** tendency (Thrombocytopenia, and decreased prothrombin)
3. **Gynecomastia** & testicular atrophy (decreased estrogen inactivation)
4. Lab investigations: elevated enzymes (SGPT, SGOT), hypo albuminaemia, lowered prothrombin

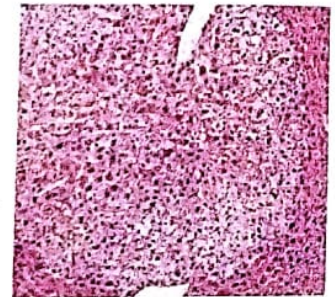


N.B. **Cirrhotic regression**: restoration of liver function is possible after cirrhosis. Not all cases progress into liver failure. But regression of fibrosis does not occur. **Cirrhosis is irreversible**.

Tumors of the Liver

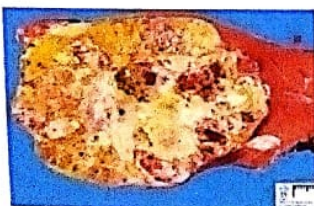
• Benign

- **Cavernous Hemangioma** (*the most common*)
 - Mass of vascular spaces, lined by endothelium
 - May be Asymptomatic – Pain - Hemorrhage
- **Liver cell Adenoma** (predisposed by contraceptive pills)
 - Rounded pale yellow or green
 - Solid Cords of normal hepatocytes. No portal tracts or C.V.
- **Bile duct Adenoma** males, small tumor, (ducts+stroma)



• Malignant

- **1ry**
 - **HCC** *the most common 1ry malignant*
 - **Cholangiocarcinoma** (old age)
 - P.F.: 1ry **sclerosing cholangitis**, **Fibrocystic** dis, **Thorotrast**
 - Origin: intrahepatic bile ducts
 - Gross: **Hard white** mass
 - Micro: Adenocarcinoma with excess fibrous desmoplasia
 - **Angiosarcoma**
 - Multiple hemorrhagic masses
 - anastomosing vessels + malignant endothelial cells

**Hepatoblastoma**

- Embryonic tumor in **children**
- **Capsulated** mass in right lobe. Areas of necrosis & hemorrhage
- Forming malignant **epithelial** (fetal or embryonic hepatocytes) + **mesenchymal** component

○ **2ry (Metastatic)** *more common than 1ry*

- Direct, retrograde **lymphatic**, **hepatic artery** (systemic tumors), **portal vein** (GIT tumors)
- Gross: enlarged liver, multiple nodular, **umbilicated** (central necrosis) **grayish**, or **brown** (in melanoma & choriocarcinoma)



Hepatocellular carcinoma

Incidence: more in males >40y

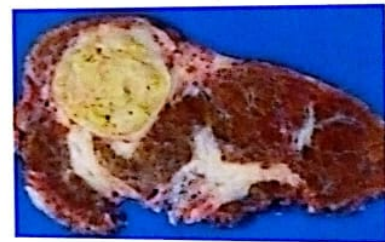
P.F.:

- **HBV** (directly oncogenic)
- **HCV**
- Aflatoxin (Aspergillus fungal toxin in moldy grains → mutation of P53)
- Other causes (Alcohol, Alpha1 ATD, Hereditary hemochromatosis & tyrosinemia)
- Genetic (B-catenin, P53)

P.L.: **Dysplasia** (small cell dysplasia) - Macronodular **cirrhosis**

Gross: Liver size is **enlarged**. Tumor is pale or **green**. Soft with areas of **N/H**.

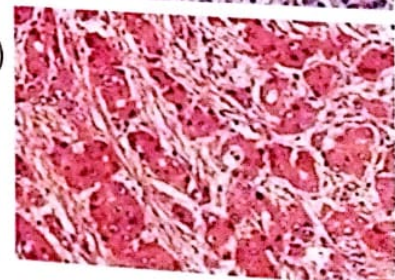
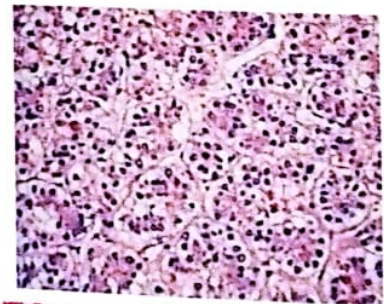
- Single unifocal (Large mass)
- Multifocal (nodules)
- Diffuse infiltrative



Microscopic types:

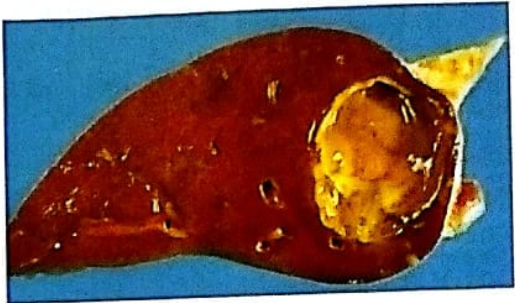
Malignant cells are similar to normal hepatocytes, or may show Anaplasia, arranged in:

- **Well differentiated** (hepatocytes with little stroma)
 - **Acinar** pattern (pseudo glandular)
 - **Trabecular** (thick cell plate >3 cells)
 - **Mixed**
- **Fibro-lamellar**: **Not predisposed** by Cirrhosis or HCV
nests or cords separated by dense collagen:
(not related to hepatitis – Young age – better prognosis)
- **High grade**: large anaplastic cells



Diagnosis is confirmed by CT & elevated alpha Fetoprotein

Liver Abscess

Amoebic abscess (sterile)	Pyogenic abscesses
Following intestinal amebiasis → portal spread	<u>Systemic</u> pyemia or <u>portal</u> pyemia <u>Ascending</u> cholangitis (suppurative Cholecystitis + stone) <u>Actinomycosis</u> <u>Ameobic</u> or hydatid (complicated)
Gross: <u>Single</u> cavity (50%) – <u>right</u> lobe – <u>irregular</u> wall – grayish brown (<i>Anchovy sauce</i>) Chronic abscess has smooth wall 	Irregular cavities containing yellow pus In ascending cholangitis : multiple yellow foci 
Micro: <u>Necrotic</u> liver cells + <u>ameba</u> with clear halo+ <u>inflammatory</u> cells G.T. & fibrosis	Micro: Pus In ascending cholangitis : pus inside <u>dilated</u> bile ducts
Fate: Compression (elevated enzymes- jaundice- pleural effusion due to lymphatic compression) Rupture (into Colon or Stomach – Into peritoneum → peritonitis) Spread (systemic infection)	

Jaundice

Yellow discoloration of Skin, sclera, & m.m. Due to increased serum **bilirubin > 2-3 mg/dl**
 (normal 0.2 – 1.2)

Types of jaundice: Haemolytic – Hepatocellular – Obstructive

Pathogenesis:

Unconjugated hyperbilirubenemia	Conjugated hyperbilirubenemia
- Hemolytic anaemia -Decreased liver uptake (e.g. Rifampicin) -Decreased conjugation (newborn)	-Decreased excretion by liver (hepatitis , toxins) - I.H. biliary obstruction (hepatitis, 1ry biliary cirrhosis, drugs) - E.H. biliary obstruction (C I S T)

Acute cholecystitis

Aetiology: **Calcular** (stone) – **Acalcular** (Infection, trauma, burn, Rheumatoid)

Gross:

Size: **enlarged** Surface: Fibro-purulent C/S: thick wall, may show stones(90%)
mucosa: congested, **ulcerated** . rarely **Empyema**, or **gangrene**

Micro:

mucosa: intact or ulcerated wall: edema+**neutrophils** (may show gangrenous necrosis)



Chronic cholecystitis

Aetiology: following attacks acute non calcular - **Stone** (Calcular) the most common

Gross:

Size: normal or **reduced** Surface: **fibrous** adhesions C/S: **thick** fibrotic wall, contain stone
mucosa: atrophic, ulcerated or intact

Micro:

mucosa: normal - ulcerated – atrophy – **hyperplasia** -**squamous metaplasia**

Wall: Chronic inflam. Cells + invaginated glands (**Rokitansky aschoff sinus**) + fibrosis

Hydrops: G.B. is obstructed and filled with clear fluid.

Mucocele: distended with mucin.

Cholelithiasis: accumulation of cholestol-laden macrophage → **Strawberry G.B.** (red and yellow)

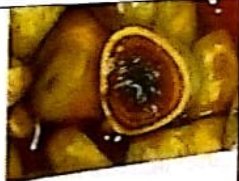
Gall bladder stones (cholelithiasis)

Complications of G.B. stone:

- **Cholecystitis**
 - Squamous metaplasia → Carcinoma
 - Perforation → fistule with intestine → **stone ileus** → intestinal obstruction
- Obstruction of **cystic duct** :
 - Biliary colic
 - **Hydrops** or **Mucocele** or **empyema**
- Obstruction of **CBD** :
 - **Obstructive jaundice**
 - **2ry biliary cirrhosis**
- **Ampulary** obstruction → Acute hemorrhagic pancreatitis



Types of G.B. stones

	Cholestrol		Pigment	
	Pure	Mixed	Black	Brown
Incidence	10%	80%	10%	
P.F.	Excess cholesterol (Feales, contraceptive pills) decreased Bile salts		Hemolytic anemia	
Composition	90% cholesterol	Cholesterol Pigment (Ca billirubinate), Ca salts (carbonate) Protein	Pigment (Ca billirubinate) Ca salts (carbonate)	Pigment (Ca billirubinate) Ca Stearate
Number	<u>Single</u>	multiple	multiple	multiple
Gross	Size: up to 4 cm Shape: rounded Surface: mulberry C/S: crystalline Color: pale - yellow	1-2 cm Faceted Smooth Laminated yellowish brown	Mm irregular friable Glossy Shiny black	Mm irregular friable Laminated Dull brown
				
Radiodensity	Radiolucent	<u>Radio opaque</u>	<u>Radio opaque</u> 50%	Radiolucent
Effect on G.B.	Cholestrololosis	Cholecystitis	Cholecystitis	Cholecystitis

Tumors of Gall bladder**Benign:**

- Adenoma: Tubular – Villous – Tubulovillous
- Adeno-myoma : proliferated smooth muscle + reactive glands (in cholecystitis)

Malignant:

- Carcinoma of gall bladder
 - Females >60 y . P.F.: stones
 - Infiltrative thickening in fundus - or fungating
 - Adenocarcinoma (papillary)– Squamous C. C.

Pancreatitis

	Acute	Chronic
Def	Acute inflammation with acinar cell injury	Progressive destruction followed by fibrosis
Aetiology	-Metabolic (Alcohol, lipoprotein, Ca) -Mechanical (Stone – Surgical trauma) -Infections (e.g. Mumps, Coxsackie) -Ischemic (Shock, embolus, PAN) -Idiopathic (20%) -Genetic (mutation in Trypsin inhibitor)	-Alcohol -Stones - Cystic fibrosis (obstructed duct) -Familial & genetic (e.g. Tropical)
Pathogenesis	-Duct obstruction & direct acinar injury → Activation of enzymes: -Amylase → liberated in blood (diagnostic) -Lipase → fat necrosis & calcification -Elastase → tissue destruction -Trypsin → activate Proteases, Kinin, & Hageman factor & leads to: -Inflammation & edema -Pancreatic necrosis -Vascular damage → hemorrhage -DIC	Alcohol leads to: 1- protein secretion → duct obstruction 2- Acinar cell fatty changes 3- Increased F.R. → inflammation & fibrosis
Gross	-Large, edematous -Hemorrhage -Chalky white foci (fat necrosis) 	-Hard fibrotic -Obstructed dilated ducts 
Micro	-Acute inflammation -Pancreatic Necrosis (panlobular) + hemorrhage -Fat necrosis & dystrophic calcification -Vascular thrombosis	-Chronic inflammation (periductal & perilobular) -Acinar fibrosis -Duct dilatation (contains plug) -Duct : atrophy, hyperplasia, metaplasia -Pseudocyst
C/P	-Epigastric pain → radiating to the back -elevated (Amylase & lipase), hypocalcaemia -Shock (bleeding, release of mediators Pg, BradK.) -Radiology → large	Asymptomatic/ repeated attacks of pain -requires C.T. scan
Complications	-DIC -Pancreatic Abscess -Pancreatic pseudocyst -Death (ARDS, DIC, Renal failure)	-Malabsorption & steatorrhea -2ry D.M.

Tumors of Pancreas

• Cystic tumors

- Mucinous cystadenoma – Mucinous cystadenocarcinoma
- Serous cystadenoma
- Papillary cystic tumor (*low grade malignant. More in girls*)



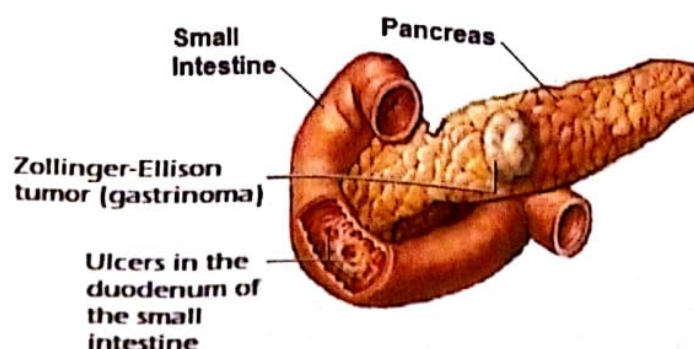
• Carcinoma

- Incidence: males >60 y
- P.F.: **Smoking** – **D.M.** – Chronic **pancreatitis** – Familial (**K-RAS**, P53 mutations)
- Sites: **Head** 60% - Body & tail 20% - Diffuse 20%
- Gross: grayish hard mass (In head → ampullary obstruction & biliary dilatation)
- Micro:
 - Adenocarcinoma (moderate or poor) + **dense fibrous stroma**
 - Adenosquamous
- C/P:
 - Asymptomatic/ Pain
 - Migratory thrombo-phlebitis (**Trousseau's syndrome**)
 - In Head → **obstructive jaundice**
 - Body & tail → Silent
 - Tumor markers: CEA, **CA19-9**



• Endocrine tumors

- Alpha cell tumor (**A**) → glucagon → D.M. – necrotizing erythema & anemia
- Beta cell tumor (**B**) mostly benign adenoma 95% → Insulin → hypoglycemia
- Delta cell tumor (**D**) → Somatostatin
- "**G**" cell **Gastrinoma** (Zollinger Ellison):
 - Secrete **Gastrin**
 - 60% malignant
 - Sites: Body & tail – **extrapancreatic** (duodenum gastric antrum)
 - **Triad**:
 - Gastrinoma
 - Gastric **hyperacidity**
 - peptic **ulcers** (gastric, duodenal, & jejunal)



- 1- Piece-meal necrosis means necrosis of:
 - a. Single liver cells.
 - b. A limited zone of hepatic lobule.
 - c. Groups of liver cells in the hepatic lobule.
 - d. Hepatocytes at the limiting plate between the parenchyma and portal tract.
- 2- The type of hepatocyte necrosis in viral hepatitis is:
 - a. Focal necrosis.
 - b. Piece-meal necrosis.
 - c. Bridging necrosis.
 - d. Any of the above
 - e. None of the above.
- 3- The following type of hepatic necrosis is characteristic of acute yellow atrophy:
 - a. Focal necrosis.
 - b. Zonal necrosis.
 - c. Piece-meal necrosis.
 - d. Bridging necrosis.
 - e. Massive hepatic necrosis.
- 4- A 52-year-old alcoholic hypertensive male presents with chronic liver disease. He has been on hypertensive drugs for 3 years. Liver biopsy reveals fatty change, cholestasis eosinophils and non caseating epithelioid granuloma. What is the most likely diagnosis?
 - a. Alcoholic hepatitis.
 - b. Drug induced hepatitis.
 - c. Autoimmune hepatitis.
 - d. Chronic persistent hepatitis.
- 5- A 25-year-old man noted abdominal cramps for four weeks. His stool was positive for mucus and blood. Ultrasound reveals a cystic lesion in the liver. Aspirate of the cyst reveals pasty greyish-brown material with streaks of blood.
 - a. What is the most likely diagnosis?
 - b. List the possible complications of this cyst?
 - c. What is the cause of abdominal pain and its relation to the liver cyst?
 - d. State another cystic lesion in the liver and mention 2 differences between the 2 cysts.
- 6- Chronic hepatitis occurs in case of infection by all except:
 - a. Hepatitis A
 - b. Hepatitis B
 - c. Hepatitis C
 - d. Hepatitis D
- 7- Acidophil bodies are:
 - a. Calcium deposits.
 - b. Immunoglobulin deposits.
 - c. Fat droplets.
 - d. Apoptotic bodies.
 - e. Amyloid deposits.
- 8- A 60-year-old woman has experienced gradual increasing malaise, jaundice & loss of appetite for the past 6 months. On examination she had mild upper quadrant tenderness. The liver enzymes were elevated. Liver biopsy revealed interface hepatitis with portal bridging fibrosis & lymphocytic infiltration in portal tract with lymphoid follicle formation. These findings are typical for which of the following?
 - a. Wilson's disease.

- b. Hemochromatosis.
 - c. HAV infection.
 - d. Cholelithiasis.
 - e. HCV infection.
- 9- The commonest cause of chronic viral hepatitis is:
- a. Hepatitis A
 - b. Hepatitis B
 - c. Hepatitis C
 - d. Hepatitis D
- 10- The cause of liver cell injury in viral hepatitis is:
- a. Direct cytopathic effect of the virus.
 - b. Cell-mediated immune response.
 - c. Humeral-mediated immune response.
 - d. Unknown.
- 11- An 84-year-old male is found at autopsy to have a cirrhotic liver in which the size of the liver nodules averages 2 to 3 mm. microscopically, the liver shows regenerative nodules with extensive fibrosis along with scattered lymphocytes, fatty change Mallory's bodies and bile duct proliferation. Which of the following etiologies best explains the appearance of the cirrhosis in this case?
- a. Alpha-1 antitrypsin deficiency.
 - b. Hepatitis B infection.
 - c. Biliary atresia.
 - d. Wilson's disease.
 - e. Chronic alcoholism.
- 12- A 49-year-old woman presents with increasing fatigue and is found to have elevated liver enzymes. Viral markers are not elevated. The biopsy reveals portal inflammation that focally destroys limiting plate. Anti-smooth muscle antibody and antinuclear antibody are found in patient serum.
- a. What is the possible diagnosis?
 - b. What are the microscopic features?
 - c. What is the fate of the disease?
- 13- Regarding secondary biliary cirrhosis, the following is not true:
- a. It is due to extrahepatic biliary obstruction.
 - b. It is micronodular cirrhosis.
 - c. The liver is enlarged and bile-stained.
 - d. The hepatocytes show ground glass appearance.
- 14- Cause of portal hypertension in hepatic cirrhosis:
- a. Pressure of regenerating nodules on branches of portal vein.
 - b. Destruction of branches of portal vein by fibrous tissue.
 - c. Development of anastomosis between the branches of portal vein and hepatic artery.
 - d. All of the above.
 - e. None of the above.
- 15- The most common tumor of the liver is:
- a. Liver cell adenoma.
 - b. Hepatocellular carcinoma.
 - c. Metastatic tumors.
 - d. Hepatoblastoma.
 - e. Bile duct carcinoma.

- 16- The following factors predispose to hepatocellular carcinoma except:
- Cirrhosis.
 - Aflatoxin.
 - HBV infection.
 - Schistosomal hepatic fibrosis.
 - HCV infection.
- 17- The most dangerous complication of portal hypertension is:
- Ascites.
 - Esophageal varices.
 - Piles.
 - Splenomegaly.
 - Caput medusa.
- 18- A 30 years old female presented with jaundice. Blood examination showed elevated serum bilirubin. Abdominal US revealed a cirrhotic liver. Liver biopsy showed accumulation of PAS positive Globules in the hepatocytes. The most possible diagnosis is:
- Hemochromatosis.
 - Wilson's disease.
 - $\alpha 1$ antitrypsin deficiency.
 - Alcoholic cirrhosis.
 - Primary biliary cirrhosis.
- 19- An 18 years old male presented with elevated liver enzymes. He has negative viral markers. Negative ANA and ASMA with decrease in serum level of ceruloplasmin. A liver biopsy was done and revealed deposition of brownish pigment in the hepatocytes. The most possible diagnosis is:
- Hemochromatosis.
 - Wilson's disease.
 - $\alpha 1$ antitrypsin deficiency.
 - Autoimmune hepatitis.
 - Primary biliary cirrhosis.
- 20- A 63 years old male presented with recent darkening of the skin. On examination, skin had a dark bronze color. Work up revealed signs of DM. A liver biopsy was done and revealed extensive brown deposits in the hepatocytes and kupffer cells. The most possible diagnosis is:
- Primary Hemochromatosis.
 - Wilson's disease.
 - $\alpha 1$ antitrypsin deficiency.
 - Alcoholic cirrhosis.
 - Primary biliary cirrhosis.
- 21- A 42-year-old female having a history of liver disease, presented with jaundice. Abdominal US revealed enlarged liver. With micronodulation. Laboratory investigations revealed increased titer of AMA. The most likely diagnosis is:
- Hemochromatosis.
 - Wilson's disease.
 - Chronic active hepatitis.
 - Primary biliary cirrhosis.
- 22- A 53-year-old male came to emergency department. Because of marked hematemesis that had continued for 3 hours. He had a distended abdomen with a fluid wave and the splenic tip was palpable. Which of the following liver diseases is most likely to be present in this patient:

- a. *Cholangiocarcinoma.*
- b. *Cirrhosis.*
- c. *Fatty change.*
- d. *Massive hepatic necrosis.*

23- A 30 years old man has shortness of breath for the past year. His medical history indicates that he developed marked neonatal generalized jaundice, but he has been healthy since then. A liver biopsy revealed PAS positive globules in hepatocytes. This patient is most likely at a very high risk for development of which of the following conditions?

- a. *Congestive heart failure.*
- b. *Hepatocellular carcinoma.*
- c. *Pulmonary Emphysema.*
- d. *Diabetes Mellitus.*

24- A 48-year-old female taking oral contraceptive pills for 16 years. During routine check up. Abdominal US revealed a small rounded well-circumscribed subcapsular lesion in right hepatic lobe. What is the most likely diagnosis:

- a. *Cholangiocarcinoma.*
- b. *Hepatocellular carcinoma.*
- c. *Liver cell adenoma.*
- d. *Metastasis in liver.*
- e. *Hepatoblastoma.*

25- A 45-year-old obese nonalcoholic female presents with severe abdominal pain radiating to the back. Lab results yielded increase in serum amylase & lipase with marked decrease in calcium. Which of the following is the most common cause of such condition?

- a. *Alcohol.*
- b. *Cholelithiasis.*
- c. *Viral infection.*
- d. *Hyperlipidemia.*

26- Beta cell tumor produces:

- a. *Gastrin.*
- b. *Glucagon.*
- c. *Insulin.*
- d. *All of the above.*
- e. *None of the above.*

27- A 57-year old man presents with fatigue, weight loss for several months without any GIT symptoms. Careful history reveals past history of car accident with blood transfusion. On examination, the patient has jaundice, firm nodular liver and mild ascites. Lab studies reveal elevated liver enzymes, raised bilirubin and decreased albumin.

- a. What is your most likely diagnosis?
- b. Enumerate four other possible etiologies of this disorder?
- c. What are the possible mechanisms for ascites in such case?
- d. What are the possible complications?

28- A 57-year old man presents with fatigue, weight loss for several months without any GIT symptoms. Careful history reveals past history of car accident with blood transfusion. On examination, the patient has jaundice, firm nodular liver and mild ascites. Lab studies reveal elevated liver enzymes, raised bilirubin and decreased albumin.

- a- What is your most likely diagnosis?
- b- Enumerate four other possible etiologies of this disorder?
- c- What are the possible mechanisms for ascites in such case?
- d- What are the possible complications?

29- A 57-year-old male complains of severe upper abdominal pain extending to the mid back. Examination reveals jaundice. CT reveals an abdominal mass at head of pancreas.

- o What is your diagnosis?
- o Explain cause of Jaundice.
- o What are the predisposing factors?
- o This patient also complains of swollen tender right leg.
- o What may be the explanation?

30- A 57-year-old male complains of severe upper abdominal pain extending to the mid back. Examination reveals jaundice. CT reveals an abdominal mass at head of pancreas.

- a. What is your diagnosis?
- b. Explain cause of Jaundice.
- c. What are the predisposing factors?
- d. This patient also complains of swollen tender right leg.
- e. What may be the explanation?

True or false:

- 1) Hepatitis D virus infection is always associated with HCV infection.
- 2) Bilharziasis leads to liver cirrhosis.
- 3) Ground glass appearance is a characteristic feature of HBV infection.
- 4) The most common primary hepatic tumor in children is hepatoblastoma.
- 5) In chronic active hepatitis the limiting plate is intact
- 6) Solitary gall stones are usually cholesterol stones
- 7) In hydrops of gall bladder it is distended with mucinous material
- 8) Brown stones have laminated cut section
- 9) Pigment stones of GB are usually multiple
- 10) Carcinoma of gall bladder spreads mainly by lymphatics.
- 11) Pure cholesterol stones are the commonest type of gall stones.
- 12) Excess alcohol consumption is an important cause of pancreatitis.
- 13) Destruction of the endocrine tissue of the pancreas leads to steatorrhea.
- 14) Cirrhosis is a reversible condition.
- 15) Adenocarcinoma of the pancreas usually arises from the exocrine portion

1-Aspiration of a cystic lesion in the right lobe of the liver reveals grayishbrown, pasty material, with streaks of blood, resembling Anchovy sauce. Microscopic examination of this material reveals necrotic debris but no neutrophils and no pus cells. Which of the following is the most likely diagnosis?

- a. Hepatic amoebiasis
- b. Echinococcosis
- c. Pyogenic abscess
- d. Solitary unilocular cyst
- e. Cavernous hemangioma

2-The autopsy of a 40-year-old woman reveals a subcapsular mass in the right hepatic lobe. The mass is partially encapsulated, lighter in colour and the adjacent liver parenchyma appears compressed. Histologically, the lesion is composed of normal hepatocytes, but not arranged in a lobular architecture, with absent portal tracts and central venules. Which of the following is the most important predisposing factor for this lesion?

- a. Aflatoxin exposure
- b. Hepatitis B virus infection
- c. Oral contraceptive use
- d. Steroid hormones
- e. Cirrhosis.

3-A 42-year-old previously healthy woman notes that over the past week her eyes have developed a yellowish appearance. She has had mild nausea and vomiting with passing dark urine and pale stool over the past week. She has no other major physical examination findings except for mildly enlarged tender liver. Which of the following underlying conditions is most likely to contribute to development of her icterus?

- a. Hypercholesterolemia
- b. Thrombocytopenia
- c. Metastatic carcinoma
- d. Viral hepatitis
- e. Diabetes mellitus

4-An 18-year-old male patient presents with elevated liver enzymes. He has negative viral markers, negative anti- nuclear antibody (ANA) and anti- smooth muscle antibody (ASMA) with decrease in the serum level of ceruloplasmin. Liver biopsy was done and reveals deposition of brownish pigments in the hepatocytes. The most likely diagnosis of the patient's condition is:

- a. Alpha-1 anti-trypsin deficiency
- b. Hemochromatosis
- c. Wilson's disease
- d. Primary biliary cirrhosis
- e. Autoimmune hepatitis

5-A 26-yearold woman presents to her primary care physician with fever, malaise, and "yellow eyes". She denies alcohol abuse. Physical examination reveals a mildly enlarged, tender liver. Laboratory studies reveal a markedly increased liver enzymes, increased 1gM and anti-hepatitis A titers. Which of the following is the most likely result of this infection?

- a. Cirrhosis.
- b. Complete resolution
- c. Establishment of a chronic carrier state
- d. Fulminant hepatitis
- e. Hepatocellular carcinoma

6-A 55 —year-old alcoholic man died after an illness characterized by increasing jaundice, ascites and generalized wasting. His laboratory investigations revealed hyperbilirubinemia, hypoalbuminemia, and mildly elevated liver enzymes. At autopsy the liver shows yellowish colour, greasy touch and finely nodular appearance on outer and cut surfaces. The most likely diagnosis is:

- a. Alpha-antitrypsin deficiency
- b. Cirrhosis
- c. Hepatitis A
- d. Hepatitis C
- e. Multiple metastases

7-A liver biopsy shows drop-out of hepatocytes at the limiting plate, with rosette formation and bridging necrosis. Cellular infiltration by plasma cells is detected in zone (1). The patient is positive for anti-smooth muscle antibody. What is the most likely diagnosis?

- a. Autoimmune hepatitis
- b. Chronic persistent hepatitis
- c. Cytomegalovirus hepatitis
- d. Herpes virus hepatitis

e. infectious mononucleosis

8-A cyst in the liver, is found to be surrounded by a lightly staining wall and contains larval capsules with scolices. The most likely diagnosis is:

- a. Clonorchis sinensis
- b. Echinococcus granulosus
- c. Schistosoma haematobium
- d. Schistosoma japonicum
- e. Schistosoma mansoni

9-Three weeks after a light meal at a café, a 28-year-old man develops malaise, fatigue, and loss of appetite. On physical examination, he has mild icterus. His symptoms resolve over the next 3 weeks. On returning to the café, he finds that it has been closed by the city's health department. Which of the following serologic test results is most likely to be positive in this patient?

- a. Anti-HBs
- b. IgM anti-HDV
- c. Anti-HCV
- d. IgM anti-HAV
- e. Anti-HBc

10-A 41-year-old woman who works as a tattoo artist has had increasing malaise and nausea for the past 2 weeks. On physical examination, she has icterus and mild right upper quadrant tenderness. She continues to have malaise for the next year. A liver biopsy reveals minimal hepatocyte necrosis, mild steatosis, and minimal portal bridging fibrosis. An infection with which of the following viruses is most likely to produce these findings?

- a. HAV
- b. HBV
- c. HCV
- d. HEV
- e. Co-infection with HBV and HDV

11-A 52-year-old woman has experienced malaise that has worsened during the past year. Now, physical examination reveals mild scleral icterus. There is no ascites or splenomegaly. Serologic test results are positive for IgG anti-HCV and HCV-RNA and negative for Anti-HAV, HBsAg, ANA and AMA. Her condition remains stable for month. Which of the following morphologic findings is most likely to be present in this patient's liver?

- a. Concentric "onion skin" bile duct fibrosis
- b. Copper deposition within hepatocytes
- c. Granulomatous bile duct destruction
- d. Hepatic venous thrombosis
- e. Massive Hepatocellular necrosis
- f. Microvesicular steatosis

12-A 58-year-old has experienced gradually increasing malaise, icterus, and loss of appetite for the past 6 months. On physical examination, she has generalized jaundice and sclera icterus. She has mild right upper quadrant tenderness. A liver biopsy reveals piecemeal necrosis of hepatocytes at the limiting plate with portal tract fibrosis and a mononuclear infiltrate in the portal tracts. These findings are most typical of which of the following condition?

- a. HAV infection
- b. Congestive heart failure
- c. Hemochromatosis
- d. HCV infection
- e. Metastatic breast carcinoma

13-A 53-year-old man comes to emergency department, because of marked hematemesis that has continued to the past 3 hours. He has a distended abdomen with a fluid wave and the spleen tip is palpable. Which of the following liver diseases is most likely to be present in this patient?

- a. Cirrhosis
- b. Cholangiocarcinoma
- c. Massive hepatic necrosis
- d. Fatty change
- e. HAV infection

14-A clinical study was done on patients known to be infected with various forms of infectious hepatitis including viral hepatitis A, B, C, I), E, F and G. If they are followed for five years, which of the following is most likely to be the best predictor of whether a patient will develop chronic liver disease and cirrhosis.

- a. Presence of chronic inflammatory cells in the portal tract
- b. Degree to which hepatic enzymes are elevated
- c. Length of time that hepatic enzymes remain elevated
- d. Specific form of hepatitis virus responsible for the infection.
- e. Presence of inflammatory cells in the sinusoids in liver biopsy

15-A 61-year-old man has had ascites for the past year. After paracentesis with removal of one liter of cloudy serosanguinous fluid physical examination shows a firm, nodular liver. Laboratory findings are positive for serum HbsAg and anti-HBc. He has a markedly elevated serum alpha-fetoprotein level. Which of the following hepatic lesions is most likely to be present?

- a. hepatocellular carcinoma
- b. Massive hepatocyte necrosis
- c. Marked steatosis
- d. Wilson's disease
- e. Autoimmune disease

16-A 54-year-old farmer has a history of gastrointestinal bilharziasis. He developed ascites, hepatomegaly, and splenomegaly with hematemesis. What is the most likely diagnosis?

- a. Amoebic liver abscess
- b. Portal hypertension
- c. Cholelithiasis
- d. Leukemia
- e. Chronic active hepatitis

17-A 45-year-old fatty female, has 5 children (P5+0), complaining of flatulence and indigestion, with pain in the right hypochondrium. What is the most likely diagnosis?

- a. Liver cell failure
- b. Amoebic hepatitis
- c. Gall bladder stone
- d. Cholangiocarcinoma
- e. acute viral hepatitis

18-A 48-year-old female, taking pills for 16 years. During routine checkup, abdominal ultrasound reveals a small rounded cystic lesion in right hepatic lobe. What is the most likely diagnosis?

- a. Cholangiocarcinoma
- b. Hepatocellular carcinoma
- c. Liver cell adenoma
- d. Metastasis in liver.
- e. Hepatoblastoma

19-A 67-year-old male having a history of viral hepatitis A, 15 years ago. He is alcoholic for 30 years. He complains of fatigue and hematemesis. Liver biopsy was performed for histopathology. What is the most likely diagnosis?

- a. Post viral hepatitis
- b. Alcoholic hepatitis
- c. Secondary biliary cirrhosis
- d. Hemochromatosis
- e. None of the above

20-A 42 —year-old, fatty female presents with discomfort related to the right hypochondrium. Her laboratory investigations are all within normal range. Abdominal ultrasound reveals enlargement of liver. What is the most likely diagnosis?

- a. Posthepatitic cirrhosis
- b. Fatty liver
- c. Hemochromatosis
- d. biliary cirrhosis
- e. None of the above